REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and these comments.

I. Status of Claims

With this submission, no claims have been amended, canceled, or newly added. Upon entry of this paper, therefore, claims 1-102 will be pending and claims 84-87 will be under active consideration.

II. Rejections Withdrawn

Applicants wish to thank the Examiner for withdrawing the rejections of claims under 35 U.S.C. §101.

III. Claim Rejection- 35 U.S.C. §112, second paragraph

Claims 84-87 are rejected for alleged indefiniteness. Specifically, the Office argues that the biomarkers of the instant claims are determined by the Cu(II) IMAC3 ProteinChip array format or WCX ProteinChip array format. The Office contends that the "manufacture may change these labels in the future as they create different ProteinChips with different formats." (Office Action, page 3) Therefore, the Office finds indefiniteness because the recited labels are deemed not to identify the biomarkers.

The essential inquiry pertaining to this requirement is whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity. Definiteness of claim language must be analyzed, not in a vacuum, but in light of: (A) the content of the particular application disclosure; (B) the teachings of the prior art; and (C) the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. When the examiner is satisfied that patentable subject matter is disclosed, and it is apparent to the examiner that the claims are directed to such patentable subject matter, he or she should allow claims which define the patentable subject matter with a reasonable degree of particularity and distinctness. **Some**

latitude in the manner of expression and the aptness of terms should be permitted even though the claim language is not as precise as the examiner might desire. MPEP 2173.02 (emphasis added).

A. Current Definiteness Standard

Definiteness in claims and enabling support are distinct requirements. Both are determined as of the filing date, and it is error to rely on subsequent developments and publications to find uncertainty as to terms used in a patent. "The district court considered whether certain terms would have been enabling to the public and looked to formula developments and publications occurring well after [the inventor's] filing date in reaching its conclusions under § 112. Yet, patents are written to enable those skilled in the art to practice the invention, not the public, and Section 112 speaks as of the application filing date, not as of the time of trial." *W.L. Gore & Associates v. Garlock, Inc.* 721 F.2d 1540, 1556 (Fed. Cir. 1983) (citations omitted).

"The test for definiteness is whether one skilled in the art would understand the bounds of the claim when read in light of the specification .... If the claims read in light of the specification reasonably apprise those skilled in the art of the scope of the invention, § 112 demands no more.... The degree of precision necessary for adequate claims is a function of the nature of the subject matter." *North American Vaccine, Inc. v. American Cyanamid Co.*, 7 F.3d 1571 , 28 USPQ2d 1333 (Fed. Cir. 1993), cert. denied , 511 U.S. 1069 (1994)

B. By This Standard, The Claims Are Definite

The Office attempts to argue that because the manufacturer could change the format of the ProteinChips or change the labeling of the biomarkers in the future, the current claims are indefinite. This is in error, however. As noted above, definiteness is determined from the filing date, not a future time.

The specification is clear and precise about the definition of these markers. Specifically, support for these biomarkers are given in page 2 paragraph [0006] and Figure 2, 4A and 4B of the original specification. Thus, one of skill in the art would understand the meaning of the specific biomarkers as listed in Figures 2, 4A and 4B.

In addition, Applicants provide with this response the attestations by a qualified expert in the field, to the effect that "there is no widespread understanding or concern in the field that a manufacturer may change the labeling for or the characteristics of an IMAC- or WCX-based assay in the future, as different formats are created." Declaration under 37 CFR § 1.132 of Lee Lomas ("the Lomas Declaration"), at paragraph 5. Applicants thus have addressed, via objective evidence, the Office's expressed concern that the manufacturer could change the labeling in the future.

Applicants submit that the evidence of record also supports the proposition that, as of the filing date of the application the terms as issue delineated the relevant subject matter with a reasonable degree of clarity and particularity. Applicants request reconsideration and withdraw of the rejection, therefore.

IV. Claim Rejection- 35 U.S.C. §112, first paragraph- written description

Claims 84-87 are rejected on the ground that their salient recitations are not described in the specification in such a way as to convey possession of the claimed invention. The Office recognizes that the specification provides "the apparent molecular weight of each of the biomarkers." (Office Action, page 4) The Office argues, however, that "applicants have not described chemical, physical or other identifying characteristics" of the biomarkers. (*Id.*, page 4) Additionally, the Office fears that the manufacturer may change the relevant labeling in the future, as the manufacturer creates ProteinChips with different formats. Applicants respectfully traverse the rejection.

As noted above, Applicants provide the Lomas Declaration as evidence that "there is no widespread understanding or concern in the field that a manufacturer may change the labeling for or the characteristics of an IMAC- or WCX-based assay in the future, as different formats are created" (paragraph 5). Accordingly, Applicants submit that this concern should be obviated.

The Office is incorrect in stating that "applicants have not described chemical, physical or other identifying characteristics [of the biomarkers]." (Office Action, page 4) Specifically, to relate the mass spectroscopic to either the first group (IMAC) or the second

group (WCX), the sample is applied to either a CU(II) IMAC3 or WCX2 chip array. IMAC stands for "immobilized metal affinity chromatography," which relies on the affinity of a target protein to a metal molecule (e.g., Fe^{3+}, Cu^{2+}, Ga^{3+}), coordinated by iminodiacetic acid or nitrilotriacetic acid ligand. (Lomas Declaration, paragraph 5) Additionally, WCX stands for "weak cationic exchange" chromatography, and relies on the charge state of a protein, determined by its pI value, in a binding buffer of defined pH (*id.*).

Accordingly, the specification provides identifying characteristics in addition to biomarker molecular weights; namely, metal ion affinity and charge state. Furthermore, use of two or more approximating techniques, as described in the specification, is commonplace in the context of rapid screening for the presence of an analyte (see Lomas Declaration, paragraph 4). This type of strategy is commonly used when methodology for unambiguously confirming analyte identity is either unavailable or too laborious for routine implementation (*id.*).

The declaration evidence also substantiates that the specification describes a method routinely used to generate a physical/chemical "signature," employed to validate biomarkers:

> during a biomarker discovery phase, candidate markers are enriched and detected from a complex sample, using a physical/chemical 'signature' that is based on their chromatographic binding characteristic and their unique mass. Although other methods eventually may be employed to fix the identity of these markers unambiguously, a combination of their physical/chemical signatures provides sufficient information to infer identity in routine analysis…utilizing a combination of IMAC, WCX and SELDI signatures, for example, is deemed sufficiently precise to allow for the validation of a biomarker, even in the absence of a definitive identity.

Lomas Declaration, paragraph 6.

By the same token, it is apparent that the claims describe a defined structure, characterized by a defined biological activity. Moreover, the methodology underlying the salient claim recitations is routinely used to validate biomarkers in the relevant art. Thus, Applicants submit that a knowledgeable reader of the specification would have no reasonable doubt that they were in possession of the claimed invention when the application was filed. Accordingly, reconsideration and withdrawal of this Section 112 rejection are requested.

V. Claim Rejection- 35 U.S.C. §112, first paragraph- enablement

Claims 84-87 are rejected for an alleged lack of enabling support in the specification as filed. In particular, the Office argues that only the "WM-446 and WM-447 are identified as markers capable of identifying lunch cancer by themselves (paragraph 0011)." (Office Action, page 6) Furthermore, the Office argues that the "specification does not teach or show working examples of using the other biomarkers identifying lunch carcinoma by themselves" (*id.*).

A. Current Enablement Standard

The courts have interpreted the enablement requirement to require that the specification teach those in the art to make and use the invention without "undue experimentation." As set out in *In re Wands*, 858 F.2d 731, 737; 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), the factors to be considered in determining whether required experimentation is undue include: 1) the breadth of the claims; 2) the nature of the invention; 3) the state of the prior art; 4) the level of a person of ordinary skill; 5) the level of predictability in the art; 6) The amount of direction provided by the inventor; 7) the existence of working examples in the specification; and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The courts have pointed out that "[n]ot every last detail [of an invention need] be described [in a patent specification], else patent specifications would turn into production specifications, which they were never intended to be." *In re Gay,* 135 USPQ 311,316 (C.C.P.A. 1962). Citing the opinion in *In re Gay,* the PTO Board of Patent Appeals and Interferences echoed this point in its statement that" the law does not require a specification to be a blueprint to satisfy the requirement for enablement under 35 U.S.C. 112, first paragraph." *Staehelin v. Secher*, 24 USPQ2d 1513, 1516 (Bd. Pat. App. & Int. 1992). Even more generally, the Office's rules state that the specification need not disclose what is well known to those skilled in the art and preferably omits that which is well known to those skilled and already available to the public. MPEP § 2164.05(a).

Pursuant to MPEP § 2164.04, the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. *In re Wright,*

999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993) (examiner must provide a reasonable explanation as to why the scope of protection provided by a claim is not adequately enabled by the disclosure). A specification disclosure that contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. Furthermore, the "examiner must then weigh all the evidence before him or her, including the specification and any new evidence supplied by applicant with the evidence and/or sound scientific reasoning previously presented in the rejection and decide whether the claimed invention is enabled. The examiner should **never** make the determination based on personal opinion. The determination should always be based on the weight of **all** the evidence." MPEP § 2164.05 (original emphasis).

B. By This Standard, The Claims Are Enabled

Claim 84 is directed to a computer-readable medium having computer-executable instructions for performing a method of qualifying lunch carcinoma status in a subject. The breath of the claims are narrowly tailored to the specific biomarkers listed in the claims. The nature of the invention is relatively straightforward, in that it uses specific biomarkers correlated to lung cancer. It is submitted that the level of ordinary skill in the relevant art, is relatively high. Furthermore, the level of predictability in the art is high, in fact, using the invention, there is a 85% or greater sensitivity and specificity are determined (Specification, paragraph [0056]). The quantity of experimentation needed to make or use the invention is minimal, as discussed below.

Applicants believe the Office has overlooked relevant data in the specification. Table 1 and Table 2 on pages 14-16 provide specific decision trees associated with the top 50 biomarkers. As the Office correctly notes, WM-446 are WM-447 the only 1-node WCX markers used to determine lung cancer; that is, the presence of either WM-446 or WM-447 is associated with lung cancer. Table 2 discloses, however, the biomarkers associated with 2 nodes, 3 nodes, 4 nodes, 5 nodes and 6 nodes, respectively. In other words, the specification expressly teaches an association of lung cancer with the presence of these 2, 3, 4, 5 and 6

biomarkers, respectively. Similarly significant is the disclosure, in Table 1, of IMAC biomarkers associated with 2 nodes, 3 nodes, 4 nodes and 5 nodes.

In light of the foregoing, Applicants submit that all of the *Wand* factors militate in favor of the enabled quality of the present claims. Accordingly, Applicants respectfully request reconsideration and withdrawal of this Section 112 rejection.

CONCLUSIONS

Applicants submit that this application is in condition for allowance, and they request an early indication to this effect. Examiner Lin is invited to contact the undersigned directly, should he feel that any issue warrants further consideration.

The Commissioner is hereby authorized to charge any additional fees, which may be required under 37 C.F.R. §§ 1.16-1.17, and to credit any overpayment to Deposit Account No. 19-0741. Should no proper payment accompany this response, then the Commissioner is authorized to charge the unpaid amount to the same deposit account. If any extension is needed for timely acceptance of submitted papers, Applicants hereby petition for such extension under 37 C.F.R. § 1.136 and authorize payment of the relevant fee(s) from the deposit account.

Respectfully submitted,

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